

Chapter 1

Introduction

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Abstract Dendrites are cellular structures essential for the integration of neuronal information. The immense variety but stereotypic architecture of dendritic arbors across the nervous system, have long suggested that dendritic structure and function are organized to meet the processing needs unique to each circuit. Technological advances have greatly pushed the frontiers in research on dendrites at macroscopic and microscopic levels. As such, there has been increasing efforts and knowledge gained in elucidating the structural, functional and molecular mechanisms that regulate the development of dendritic arbors, and that maintain their form and function throughout life. Moreover, as we seek to repair the damaged nervous system, it is clear that a better understanding of how dendrites are perturbed in neurodegenerative disease is needed. In this book, we introduce the basic biology of dendrites, and discuss current knowledge of the mechanisms that control cellular, molecular and functional aspects of dendritic development and maintenance in health and in disease.

Dendrites are the essential substrate for receiving and integrating neuronal information. These elegant but complex structures have been studied for more than a century since their visualization using cellular staining methods devised in the late nineteenth century by Camillo Golgi (Fig. 1.1a; Golgi 1873). Santiago Ramon y Cajal's (1899–1904) initial and insightful definition of the role of dendrites in neuronal processing was borne out by electrophysiological investigations that became feasible in the mid-1900s. Since then, an entire field has evolved – the study of dendritic structure

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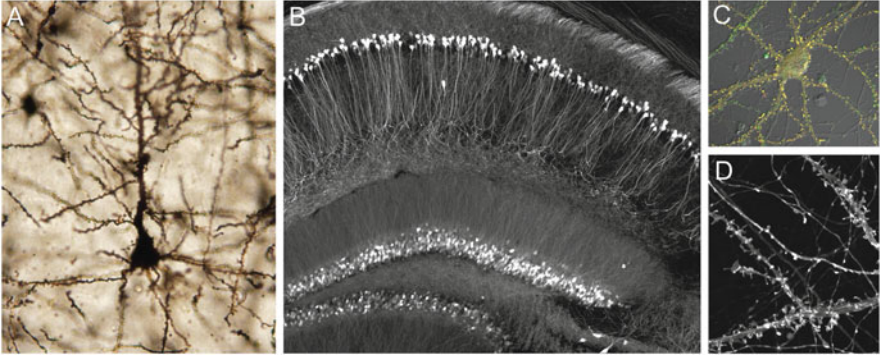


Fig. 1.1 (a) Cortical neuron labeled by the Golgi method (provided by E. Huang). (b) Dendritic arbors of adult hippocampal neurons in transgenic mice expressing yellow fluorescent protein. Confocal microscopy reconstruction from a brain slice (provided by H. Okawa, K. Oda, and R. Wong). (c) An image of a hippocampal neuron in culture immunostained with antibodies against two postsynaptic scaffolding proteins, PSD-95 (*green*) and Homer (*red*) (provided by S. Okabe). Fluorescence images were overlaid with a DIC (differential interference contrast) image. (d) Dendritic spines of hippocampal neurons in culture expressing myristoylated alanine-rich protein kinase C substrate (1–40) tagged with GFP (Marcks-GFP) to highlight the plasma membrane (provided by C. Hoogenraad). *Source*: A cover picture of the journal (*Microscopy* vol 62, no 1, 2013)

and function is now one of the leading areas of investigation in basic and translational neuroscience research. In this book, we wish to bring together current knowledge of how dendrites gain their unique and necessary cellular architecture and connectivity during development, as well as highlight how a failure to attain or maintain these attributes result in devastating disease. It is our hope that the reader will find new comprehension and appreciation for the many strategies that neurons engage to assemble and maintain their dendritic structure and function, and thus the workings of the nervous system, throughout life.

Dendritic arbors are highly patterned across the nervous system, but vary tremendously in their size and fine architecture, each designed to best serve specific computations within their networks. Despite the immense diversity in architecture, dendritic arbors of neurons from each region of the nervous system are stereotypic in their branching patterns and synaptic organization. Such stereotypic patterns make dendrites highly amenable for studies across animals, as well as in tissue explants and in dissociated cell culture in which major features of dendrites are preserved (Fig. 1.1b–d). Both *in vivo* and *in vitro* studies have greatly illuminated the cytoskeletal organization and cell biological processes that dendrites depend on in order to perform properly. Also, much is now known about the cellular interactions and molecules that pattern individual dendritic arbors as well as regulate their spatial arrangements across their populations. Importantly, *in vivo* and *in vitro* approaches have in parallel greatly increased our understanding of the structure and function of synapses onto dendrites, as well as the computations that result from these inputs. Proper development of dendrites is thus an essential step in the establishment of

neuronal connectivity and function. Equally important is the maintenance of dendrites and their connectivity, a process that is seriously disrupted in neurological disease.

By comparing dendritic morphologies across ages, Cajal was able to describe the successive stages in the development of dendrites and their connectivity. Over the past several decades, many molecular mechanisms that control dendrite development and maintenance have been revealed, largely due to technical advances in cell and molecular biology. High-resolution imaging of living neurons expressing various fluorescent protein-tagged reporters, together with calcium imaging and electrophysiological recording, has greatly facilitated simultaneous real-time monitoring of morphological and functional changes in dendrites in response to physiological stimuli. Methods to introduce or manipulate genes of interest in specific neuronal cell types or entire networks of cells are also improving continuously. These methods are also being applied to elucidate the changes in dendrites in many neurological diseases, either as a consequence of developmental defects or due to the failure in maintaining the circuits that have formed. The chapters in this book aim to relay how such diverse approaches have been applied to generate a comprehensive understanding of the cellular and molecular mechanisms responsible for shaping the form and function of dendrites.

The authors of this book describe recent work that we have grouped into five major themes, which collectively cover a wide array of topics that we hope will provide the reader with a broad, but sufficiently detailed, view of dendrite development and disruption in disease. The chapters will highlight work across species including flies, frogs, and rodents. In Chaps. 2, 3, 4, 5, 6, and 7, we focus on several major aspects of the “cell biology” of dendrites, including their cytoskeletal organization, the trafficking of proteins, and the signals that convey input at dendrites to the cell nucleus to generate longer-term regulation of neuronal function (Fig. 1.2, Cell biology). The next theme (Chaps. 8, 9, 10, and 11) directs the reader’s attention to the stereotypic architectural arrangements of dendritic arbors, which are designed to execute specific functions of the respective cell types. In particular, the authors underscore the basic rules that govern dendrite branching patterns and review how specific branching patterns relate to function (Fig. 1.2, Patterning). Then, in Chaps. 12, 13, and 14, we lead the reader to current findings unraveling the cellular and molecular control of dendrite morphology. Chapters 15, 16, 17, 18, and 19 discuss many aspects of the development and maturation of synaptic connections onto dendrites (Fig. 1.2, Connectivity). This block of chapters emphasizes a variety of molecular, imaging, and electrophysiological techniques that are used to unravel the mechanisms that govern synapse assembly on dendrites. Finally, in Chaps. 20, 21, and 22, we consider dendritic organization in common neurological diseases: autism, amyotrophic lateral sclerosis, frontotemporal dementia, and glaucoma. The discussions in these disease models hopefully will lead to more discoveries in the future of the critical role of dendritic growth and maintenance in neurodevelopmental and neurodegenerative diseases.

We thank the authors for their dedication and excellent contributions to the book, without which this project would not have been possible. We hope that the book will provide novel information to students and established investigators alike,

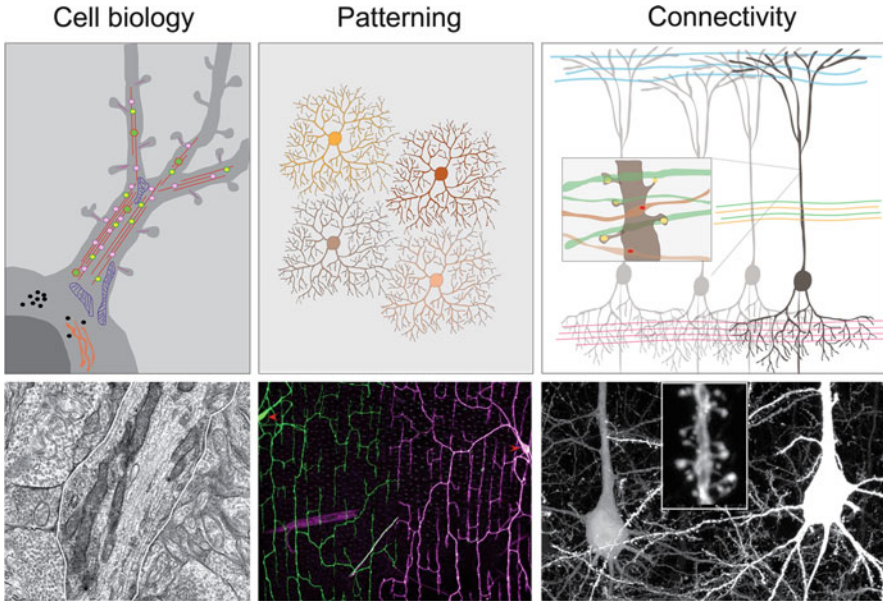


Fig. 1.2 Schematics and an example showing the major organizational plans of dendrites covered in the chapters of this book: cell biological organization and processes, patterning of dendritic arbors, and global and local arrangements of synaptic connectivity. *Cell biology*: The cytoskeleton and trafficking of proteins to and away from the cell body are essential for dendrite maintenance and function. Image: Transmission electron microscopy showing ultrastructure of a mouse retinal ganglion cell dendrite (outlined; provided by A. Bleckert and R. Wong). *Patterning*: Dendrites of individual neurons do not cross each other (self-avoidance), and in some systems, dendritic arbors of cell-like types tile. Image: *Drosophila* sensory neurons labeled genetically, showing “self-avoidance” and tiling (provided by K. Emoto). *Connectivity*: Dendritic arbors are contacted by many types of inputs (colored differently), which are distributed in stereotypic patterns across the cell and also at the level of individual synapses. Inset shows excitatory connections in green/yellow on spiny protrusions on the dendrites and inhibitory connections in red on dendritic “shafts,” smooth portions of dendrites. Image: Dendrites of fluorescent protein expressing cortical neurons from a transgenic line; inset shows spines (provided by H. Okawa, K. Oda, and R. Wong)

as well as to clinicians interested in the basic pathology of dendrite degeneration. We also hope that the many concepts and ideas presented in the book will contribute toward escalating research on this crucial compartment of the neuron.

References

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